Structure and Characteristics of Hydroxyapatite/Dexamethasone-loaded PLA Bilayered Scaffold for Bone Regeneration

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Statement of Purpose: Polylactide (PLA) is popularly used for fabrication of biodegradable scaffolds due to their biocompatibility and proven biodegradability. The ability for PLA scaffolds to be used for bone tissue regeneration was also shown to be enhanced by a coating of bone-like apatite layer [1].

In addition to PLA scaffolds, hydroxyapatite (HAp) porous scaffolds have also been used for bone tissue regeneration. HAp is biocompatible since it is found in the inorganic portion of bone and that it possesses osteoconductive properties [2]. In this study, the bone-like apatite-coated HAp/dexamethasone (DEX)-loaded PLA bilayered porous scaffolds were fabricated using a combination of template-coating and particle leaching/gas forming techniques. In order to mimic normal bone structures, the outside cortical-like shells fabricated of porous HAp, whereas the trabecular-like core was made of porous PLA. The physical and biological properties of fabricated bilayered scaffolds were compared to pure HAp porous scaffold.

Materials and Methods: Cortical-like HAp scaffolds with hollow in its inside was fabricated using a polyurethane sponge template. The template sponge was coated with HAp water-based slurry containing binders, dried, and followed by sintering at 1230℃. The dimensions of the fabricated HAp scaffold shells have an outer diameter of 10 mm, a height of 5 mm, and an inner diameter of 6 mm (Fig. 1A).

Trabecular-like porous PLA scaffolds containing DEX was directly formed by a particle leaching/gas forming method with sodium percarbonate as a novel porogen in the inner diameter of HAp scaffolds. Oxygen plasma treatment was performed to modify the PLA surface of bilayered scaffolds. The surface modified bilayered scaffold was then immersed in simulated body fluid (SBF) solution at 5 times ionic concentration for 24 hr to obtain the final bone-like apatite-coated HAp-DEX-loaded PLA bilayered porous scaffolds (Fig. 1B).

Physical properties of the bilayered composite scaffold were analyzed by helium pycnometry, SEM, and micro CT, whereas the biological responses to the scaffolds were evaluated using human embryonic palatal mesenchymal (HEPM) cells, an osteoblast precursor cell line. After 7, 14, 21 and 28 days of culture, total protein, dsDNA, alkaline phosphatase (ALP) specific activity cells in bilayered scaffold were measured and the biological responses were compared with pure HAp porous scaffolds.

Results and Discussion: From the micro CT images, it was observed that the fabricated bilayered scaffolds contain open and interconnected pore structures, with no structural delaminations on the external surfaces (Fig. 1B, C, and D). Using helium pycnometry, the maximum porosity was observed to be greater than 90% and the corresponding average pore size for the PLA scaffolds was observed to be in the range of 100 to 700 μm. In addition, SEM images shown that dense and uniform bone-like apatite layer was successfully formed on the surface of bilayered scaffolds (Fig. 1E and F).

In an attempt to develop a more biomimetic scaffold for bone regeneration, novel bilayer scaffold consisting of cortical-like porous HAp and DEX-loaded trabecular-like porous PLA scaffolds was investigated in this study. The rationale for this design is that this the bilayered scaffolds can act as a delivery vehicle for drugs such as the DEX, which is a bioactive molecular capable of stimulating the effective expansion and differentiation of stem cells.

From this study, novel bilayered scaffold loaded with DEX was shown to enhance HEPM cell attachment, proliferation and viability when compared to control HAp porous scaffolds (Fig. 1G, H, and I). It was thus suggested that the released Dex from PLA in bilayered scaffold promoted the osteogenesis of the HPEM cells.

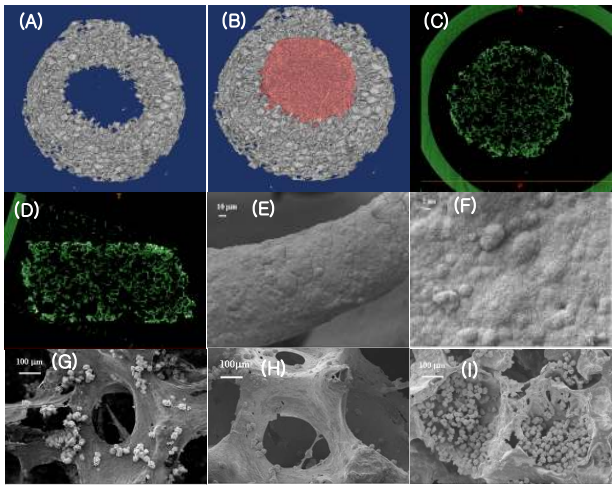

Figure 1. Micro CT and SEM images of bone-like apatite-coated HAp/DEX-loaded PLA bilayered scaffold: (A) and (B) 3D images of HAp and bilayered scaffold; (C) and (D) surface and cross-section images of PLA in bilayered scaffold; (E) and (F) surface of apatite-coated HAp and PLA; (G), (H), and (I) 2 weeks HEPM cell culture of control HAp, HAp and PLA of bilayered scaffold.

References:

1. Zhang R, et al., J Biomed Mater Res. 1999;45:285-293.
2. Appleford MR, et al., Biomaterials 2007;28:2747-2753.